CLAIMS

1. A method of determining whether a patient has, or is responding to treatment for, cystic fibrosis the method comprising the steps of (1) obtaining a suitable epithelial cell sample from the patient, (2) determining whether nucleotide diphosphate kinase (NDPK) function or state is altered compared to its function or state in a control epithelial cell.

2. A method according to Claim 1 wherein phosphorylation of NDPK is altered.

3. A method according to Claim 1 wherein nucleoside triphoshate production from a given nucleoside diphosphate is measured.

4. A method of determining whether a patient has, or is responding to treatment for, cystic fibrosis the method comprising the steps of (1) obtaining a suitable epithelial cell sample from the patient, (2) determining whether histidine phosphorylation of annexin is altered compared to its phosphorylation in a control epithelial cell.

5. A method according to Claim 4 wherein the histidine is His246 or His293 of annexin.

6. A method according to any one of Claims 1 to 5 wherein the epithelial cell sample from the patient is a lung cell sample or a nasal cell sample.

7. A method of classifying a disease state associated with epithelial cell dysfunction in a patient, the method comprising (1) obtaining a suitable epithelial cell sample from the patient and (2) determining for one or more of the following whether the measured parameter is altered compared to a control epithelial cell the measured parameters being: (i) nucleoside diphosphate kinase (NDPK) function, (ii) phosphorylation of annexin, (iii) phosphorylation of other membrane proteins, and (iv) ATPase activity.

8. A method according to Claim 7 wherein in step (ii) phosphorylation of annexin at His246 or His293 is measured.

9. A method according to Claim 7 wherein each of parameters (i) and (ii) are measured in the sample from the patient and compared to the control sample.

10. A method according to Claim 7 wherein each of parameters (i), (ii) and (iii) are measured in the sample from the patient and compared to the control sample.

11. A method according to Claim 7 wherein all of parameters (i) to (iv) are measured in the sample from the patient and compared to the control sample.

12. A method according to any one of Claims 7 to 11 wherein the epithelial cell sample from the patient is a lung cell sample or a nasal cell sample.

13. A method according any one of Claims 7 to 12 wherein the effectiveness of a treatment for cystic fibrosis is being tested on the patient.

14. A method of identifying a compound useful in treating cystic fibrosis or which may aid the identification of a compound useful in treating cystic fibrosis the method comprising identifying a compound which modulates or restores nucleoside diphosphate kinase activity.

15. A method according to Claim 14 wherein phosphorylation of NDPK is altered.

16. A method according to Claim 14 wherein nucleoside triphosphate production from a given nucleoside diphosphate is altered.

17. A method of identifying a compound useful in treating cystic fibrosis or which may aid the identification of a compound useful in treating cystic fibrosis the method comprising identifying a compound which modulates histidine phosphorylation of annexin.

18. A method according to Claim 17 wherein the histidine phosphorylation of annexin is at His246 or His293.

19. A method of identifying a compound useful in treating cystic fibrosis or which may aid the identification of a compound useful in treating cystic fibrosis the method comprising identifying a compound which modulates the interaction between any of cystic

fibrosis transmembrane conductance regulator protein (CFTR), nucleoside diphosphate kinase (NDPK) and annexin.

20. A method according to any one of Claims 14 to 19 wherein the method is carried out *in vivo*.

21. A method of identifying a compound useful in treating cystic fibrosis or which may aid identification of a compound useful in treating cystic fibrosis the method comprising identifying a compound which substantially changes one or more of the following parameters from the state found in a cystic fibrosis epithelial cell to the state found in a normal cell, namely (i) nucleoside diphosphate kinase (NDPK) function, (ii) phosphorylation of annexin, (iii) phosphorylation of other membrane proteins such as p11 and p116, and (iv) ATPase activity.

22. A method according to Claim 21 wherein the histidine phosphorylation of annexin is at His246 or His293.

23. A compound identified by the method of any one of Claims 14 to 22.

24. A compound according to Claim 23 for use in medicine.

25. A method of treating CF the method comprising administering to a patient a compound which modulates nucleoside diphosphate kinase activity or a compound which modulates histidine phosphorylation of annexin or a compound which modulates the interaction between

any of cystic fibrosis transmembrane conductance regulator protein (CFTR), nucleoside diphosphate kinase (NDPK) and annexin.

26. A method according to Claim 25 wherein the histidine phosphorylation of annexin is at His246 or His293.

27. Use of a compound as defined in Claim 36 in the manufacture of a medicament for treating cystic fibrosis.

28. A peptide of relative molecular mass less than 6500 comprising at least ten consecutive amino acid residues surrounding the phenylalanine 508, or at least ten consecutive residues including a portion of the region between residues 508 and 551, in the polypeptide sequence of human cystic fibrosis transmembrane regulator (CFTR), or a variant or precursor thereof.

29. A peptide according to Claim 28 having between 12 and 50 amino acid residues.

30. A peptide according to Claim 29 having between 12 and 30 amino acid residues.

31. A peptide according to Claim 30 having between 12 and 20 amino acid residues.

32. A peptide according to any one of Claims 28 to 31 which has the sequence KENIIFGVSYDEYR.

33. A peptide according to any one of Claims 28 to 32 further comprising a lipid-solubilising moiety.

34. A peptide according to Claim 33 wherein the lipid-solubilising moiety is a lipid.

35. A peptide according to Claim 33 wherein the lipid-solubilising moiety is a cholesterol.

36. A peptide according to Claims 33 or 34 wherein the lipid-solubilising moiety is a fatty acid.

37. A peptide according to Claim 36 where in the fatty acid is any one of palmitic or myristic acid.

38. A peptide according to any one of Claims 28 to 37 for use in medicine.

39. A pharmaceutical formulation comprising a peptide according to any one of Claims 28 to 37 and a pharmaceutically acceptable carrier.

40. A method of treating cystic fibrosis or a chronic sputum producing disorder the method comprising administering to the patient an effective amount of a peptide according to any one of Claims 28 to 37.

41. A method according to Claim 40 wherein the peptide is administered in a nebulised form.

42. Use of a peptide according to any one of Claims 28 to 37 in the manufacture of a medicament for treating cystic fibrosis or a chronic sputum producing disorder.

43. A peptide of relative molecular mass less than 6500 comprising at least five consecutive residues surrounding histidine 246 of annexin.

44. A peptide of relative molecular mass less than 6500 comprising at least five consecutive residues surrounding histidine 293 of annexin.

45. A peptide according to Claim 43 or 44 wherein the said histidine residue is phosphorylated.

46. A method of raising an antibody reactive with histidine phosphorylated annexin, the method comprising using a peptide according to Claim 45 as an immunogen.

47. A method according to Claim 46 wherein the said peptide is combined with a carrier or adjuvant or both.

48. An antibody obtainable by the method of Claim 46 or 47.

49. An antibody reactive against annexin phosphorylated at histidine 246 but not reactive against annexin not phosphorylated at histidine 246.

50. An antibody reactive against annexin phosphorylated at histidine 293 but not reactive against annexin not phosphorylated at histidine 293.